SDI. Clarifying this association would contribute to a more comprehensive understanding of the disease and facilitate more targeted management strategies for individuals affected by NPSLE.

O29 GUT EPITHELIAL BARRIER DYSFUNCTION IN LUPUS TRIGGERS A DIFFERENTIAL HUMORAL RESPONSE AGAINST COMMENSALS

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Background and Objective Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by persistent inflammation affecting multiple organs, including the intestine. Lupus-derived gut inflammation can alter the epithelial barrier, where millions of commensals have a dynamic interaction with the host immune system. A new feature that seems to be decisive in autoimmune pathogenesis is the gut microbiota composition and its potential role. Our purpose is to elucidate the consequences of lupus gut inflammation locally and systemically and to characterize the relationship between SLE and microbiota composition.

Methods Lupus derived gut affectation was characterised by using a TLR7-mediated model of the disease. We assessed splenomegaly and anti-dsDNA autoantibodies by ELISA and the GALT IgA response by flow cytometry and ELISA. Gut permeability was evaluated using FITC-dextran and immunofluorescent staining of claudin-1 and occludin in the gut epithelium. Systemic response against microbiota was studied by ELISA and flow cytometry. The microbiota composition was analysed by V4 16S rRNA sequencing.

Results Overexpression of TLR7 induced a 'leaky gut' state with increased gut permeability and altered distribution of tight junction proteins. These alterations happened concomitantly with the onset of the disease, as characterised by splenomegaly and anti-dsDNA autoantibodies levels. TLR7Tg mice presented greater levels of GL7+ B220+ B cells within the Peyer's patches, indicating elevated local immune activity. Specifically, disease inflammation altered the gut-associated immune response by readily increasing IgA+ B cell numbers and the levels of secreted IgA when compared with WT mice. Bacterial composition was determined, and the results revealed species differentially colonizing only the gut of TLR7Tg, being *Bacteroides acidifaciens* the most significant. Interestingly, TLR7Tg presented a differential IgM, IgA and IgG2a response against *B.acidifaciens* that was absent in WT mice. This *B.acidifaciens* response in TLR7Tg mice correlated significantly with systemic levels of total IgM and anti-dsDNA IgM.

Conclusion Altogether, we demonstrate that TLR7-induced SLE manifests by disrupting the gut barrier function and changing the gut-associated immune response and microbiota composition. This enables certain bacteria to translocate and induce a systemic immune response that could reinforce autoimmunity. Whether this immune response contributes to disease development is under investigation.

O30 ANTI-HISTONE AND ANTI-NUCLEOSOME RATHER THAN ANTI-DSDNA ANTIBODIES ASSOCIATE WITH IFN-INDUCED BIOMARKERS IN SUDANESE AND SWEDISH SLE PATIENTS

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Objective In SLE, anti-dsDNA can co-occur with autoantibodies against other chromatin components, like histones and nucleosomes. These antibodies induce type-1 Interferon production, a hallmark of SLE. We measured antinuclear antibody (ANA) sub-specificities and investigated their associations to inflammatory biomarkers including interferon-regulated chemokines.

Methods We included 93 Sudanese and 480 Swedish SLE patients and matched controls (N=104+192). Autoantibodies targeting ANA-subspecificites: dsDNA, Sm, Sm/U1RNPcomplex, U1RNP, SSA/Ro52, SSA/Ro60, SSB/La, ribosomal P, PCNA and histones were quantified in all subjects, anti-nucleosome only in the Swedish patients, with a bead-based multiplex immunoassay. Levels of 72 plasma biomarkers were determined with Proximity Extension Assay technique or ELISA.

Results Among Sudanese patients, the investigated antibodies significantly associated with 9/72 biomarkers. Anti-histone antibodies showed the strongest positive correlations with MCP-3 and S100A12 as well as with interferon I-inducible factors MCP-1 and CXCL10. Anti-dsDNA antibodies associated with CXCL10 and S100A12, but in multivariate analyses, unlike anti-histone, associations lost significance.

Among Swedish patients for MCP-1, CXCL10, SA100A12 also demonstrated stronger associations to anti-histone and anti-nucleosome antibodies, compared to anti-dsDNA and other ANA sub-specificities. In multiple regression models, anti-histone/nucleosome retained the strongest associations. When excluding anti-histone or anti-nucleosome positive patients, the associations between MCP-1/CXCL10 and anti-dsDNA were lost. In contrast, when excluding anti-dsDNA positive patients, associations with anti-histone and anti-nucleosome remained significant.

Conclusions In two cohorts of different ethnical origin, autoantibodies targeting chromatin correlate stronger with IFN-induced inflammatory biomarkers than anti-dsDNA or other ANA sub-specificities. Our results suggest that anti-histone/nucleosome autoantibodies may be main drivers of type-1 interferon activity in SLE.

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